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FIG. 1

```
GCCAAGAGTCCGCAGGATGCAGTGGACGAAGGTGTTGGGGCTGGGGCTGGCAGCTGCCCTCCTCGGGCTGGCAGCTGCCCTCCTCGGCATCATCCTCGGCCA   90
                  M  Q  W  T  K  V  L  G  L  G  A  A  A  L  L  G  I  I  L  G  H

CTTTGCCATCCCCAAAAAGCCAACTCACTGCCCCCAGGACCTGGACATCCTGGAGATCCTGGAGACCGTCATGGGGCAGCTGGATGCCCA   180
F  A  I  P  K  K  A  N  S  L  A  P  Q  D  L  D  L  E  I  L  E  T  V  M  G  Q  L  D  A  H

CAGGATCCGGGAGAACCTCAGAGAACTCTCCAGGGAGCCACACCTGGCCTCCAGCCCTCGGGATGAGGACCTGGTCCAGCTGCTGCA   270
R  I  R  E  N  L  R  E  L  S  R  E  P  H  L  A  S  S  P  R  D  E  D  L  V  Q  L  L  L  Q

GGGCTGGAAGGACCCAGAGTCAGGCCTGGACTCGGCCGAGGCCTCAACGTGCTGCTCCTAGCCAGGAGCAGCCAA   360
R  W  K  D  P  E  S  G  L  D  S  A  E  A  X  T  Y  E  V  L  L  S  F  P  S  Q  E  Q  P  N

CGTCGTGGACATCGTGGGCCCCACTGGGGGCATCATCCACTCCTGCCACCGGACTGAGGAGAACGTGACCGGGGAGCAAGGGGGCAGA   450
V  V  D  I  V  G  P  T  G  G  I  I  H  S  C  H  R  T  E  E [N] V  T  G  E  Q  G  G  P  D

TGTGGTACAACCCTATGCTGCCTATGCTCTTCTGGAACCCCACAGGGCCTCCTATGCCAAGAGGGCCGGAAGAGAGACTTTAA   540
V  V  Q  P  Y  A  A  Y  A  P  S  G  T  P  Q  G  L  L  V  Y  A  N  R  G  A  E  E  D  F  K

GGAGCTACAGACTCAGGGGCATCAAACTTGAAGGCACCATTGCCCTGACTAGGTACGGGGGCGTGGGGCGTGGAACGC   630
E  L  Q  T  Q  G  I  K  L  E  G  T  I  A  L  T  R  Y  G  G  V  G  R  G  A  K  A  V  N  A

TGGCCAAGCACGGGGTAGCTGGGGTGCTGGTGTACAGACACCCGCCGACATCAACGATGGCCTGAGCTCACCGGAAACCTTCCCAA   720
A  K  H  G  V  A  G  V  L  V  Y  T  D  P  A  D  I  N  D  G  L  S  S  P  D  E  T  F  P  N

CTCCCTGGTACCTGCCCCCTCAGGAGTGGAGCGGGTCCTACTACGAGTATTTTGGGGACCCTCTGACTCCTACCTTCCAGCCGTCCC   810
S  W  Y  L  P  P  S  G  V  E  R  G  S  Y  Y  E  Y  F  G  D  P  L  T  P  Y  L  P  A  V  P

CTCTTCCTTCCGCGTGGACCTTGCCAATGTCTCCGGATTTCCCCCAATTCTACACAGCCCATTGGCTTCCAGGATGCAAGAGACCTGCT   900
S  S  F  R  V  D  L  A [N] V  S  G  F  P  P  I  P  T  Q  P  I  G  F  Q  D  A  R  D  L  L

CTGTAACCTGCAACGGAACTTGGCCCCAGCCACCTGGCAGGAGGCACTGGGCTGCCACTACAGGTTGGGTCCCGGCTTCCGGCCTGACGG   990
C  N  L [N] G  T  L  A  P  A  T  W  Q  G  A  L  G  C  H  Y  R  L  G  P  G  F  R  P  D  G

AGACTTCCCAGCAGACAGCCAGGTGAATGTGAGCGTCTACAACCGCCTGGAGCTGAGGAACTCTTCCAACGTCCTGGGCATCATCCGTGG   1080
D  F  P  A  D  S  Q  V [N] V  S  V  Y  N  R  L  E  L  R  S  S  N  V  L  G  I  I  R  G

GGCTGTGGAGCCTGATCGCTACGTGCTGTATGGGAACCACCGAGACAGCTGGGTGCACGGGGCCGTGGACCCCAGCAGTGGCACCGCCGT   1170
A  V  E  P  D  R  Y  V  L  Y  G  N  H  R  D  S  W  V  H  G  A  V  D  P  S  S  G  T  A  V
```

FIG. 1. (CONTINUED)

```
CCTCCTGGAGCTCTCCCGTGTCTCGGGACCCTGGGCTCCTGAAGAAGGGCACCTGGCGTCCTCGCAGATCAATGTGTTTGCGAGCTGGGGGGC   1260
 L  L  E  L  S  R  V  L  G  T  L  L  K  K  G  T  W  R  P  R  R  S  I  V  F  A  S  W  G  A

TGAGGAGTTTGGGCTCATTGGCTCCACGGAATTCACAGAAGAGTTCTTCAACAAGCTGCAGGAGCGCACGGTGGCCTACATCAACGTGGA     1350
 E  E  F  G  L  I  G  S  T  E  F  T  E  E  F  F  N  K  L  Q  E  R  T  V  A  Y  I  N  V  D

CATCTCGGTGTTTGCCAACGCTACCCTTAGGGTGCAGGGACGCCCCCGTGCAGAGCGTGTCTCTGCAACCAAAGAGATCCGCTC            1440
 I  S  V  F  A  N  A  T  L  R  V  Q  G  T  P  P  V  Q  S  V  V  F  S  A  T  K  E  I  R  S

ACCAGGCCCTGGCGACCTGAGCATCTACGACAACTGGATCCGGTACTTCAACCGCAGCAGCCCGGTGTACGGCCTGGTCCCCAGCTTGGG     1530
 P  G  P  G  D  L  S  I  Y  D  N  W  I  R  Y  F  N  R  S  S  P  V  Y  G  L  V  P  S  L  G

TTTCTCGGGTGCTGGCAGCGACTATGCACCCTTCGTTCACTTCCTCGGCATCTCCTCCATGGACATTGCCTATACCTATGACCGGAGCAA     1620
 S  L  G  A  G  S  D  Y  A  P  F  V  H  F  L  G  I  S  S  M  D  I  A  Y  T  Y  D  R  S  K

GACTTCAGCCAGGATCTACCCCACCTACCACACAGCCTTTGACTATGGACACCTTGATAAGTTTCTGGACCCGGGCTTCAGCAGCCA       1710
 T  S  A  R  I  Y  P  T  Y  H  T  A  F  D  T  F  D  Y  V  D  K  F  L  D  P  G  F  S  S  H

TCAGGGCTGTGCCCGACAGCGGGGAGTGTGATTCTCCGGCTGACAGCTTCTTCCTGCCCCTCAAAGTCAGTGACTACAGTGAGAC         1800
 Q  A  V  A  R  T  A  G  S  V  I  L  R  L  S  D  S  F  F  L  P  L  K  V  S  D  Y  S  E  T

ACTCCGCAGCTTCCTGCAGGCAGCGCCAGCAAGATCTTGGGGCCCAGGCTGGCTTGCTGGAGCAGCATCAGCGGCCCTCTGGTGACTGCAGT   1890
 L  R  S  F  L  Q  A  A  Q  Q  D  L  G  A  L  L  E  Q  H  S  I  S  L  G  P  L  V  T  A  V

GGAGAAGTTTGAGGCAGAAGCTGCAGCTGCCCTTGGGCCAACGCATATCAACACTGCAGAAGGGCAGCCCTGACCCCCTGCAGTCCGGATGCT 1980
 E  K  F  E  A  E  A  A  A  L  G  Q  R  I  S  T  L  Q  K  G  S  P  D  D  P  L  Q  V  R  M  L

CAATGACCAGTTGATGCTCTTGGAACGGACCTTTCTGAACCCTAGAGCCTTCCCAGAGGAACGCTACTACAGCCATGTGCTGTGGGCACC     2070
 N  D  Q  L  M  L  L  E  R  T  F  L  N  P  R  A  F  P  E  E  R  Y  Y  S  H  V  L  W  A  P

TTCGCACGGGCTCCGTAGTCACATTCCGGGGCTATCCAATGCCTGCTCCAGGGACCAGCGGCTCGAAGCTTGGGCTGA              2160
 S  H  G  L  R  S  H  I  P  G  L  S  N  A  C  S  R  A  R  D  T  A  S  G  S  E  A  W  A  E

GGGTCCAGAGACAGCTCAGCATTCTGGTGACACAGCCCTGGAGGGTGCGGCAGCCACCCTGCGCCTTGACCCTGACCCCAGCCCTC         2250
 V  Q  R  Q  L  S  I  V  V  T  A  L  E  G  A  A  A  T  L  R  P  V  A  D  L  .

TTTCTTCAGCCCTCCCTTTACTCCGGTGCTTTATATTTACAAAGTGCTTTGTGTTTTTAAAAGTCTTTT                         2320
```

FIG.2.

```
human  MQMTKVLGLGLGAAALLGLGIILGHFAIPFKANSLAP------QDLDLEILETVHGQLDAHRIRENLRELSREPHLASSPRDEDLVQLLQ : 85
rat    MHMAKILGVGIGAAALLGLGIILGHFAIPIATEPLASSVSDSQDLDLAILDSVHGQLDASRIREMLRELSKEPHVATSARDEALVQLLLG : 90

human  RUKDPESGLDSAEAXTTEVLLSFPSCEQPNVVDIVGPTEGIIHSCHRTEENVTGECGGPDVVQPYAAYAPSGTPQELVYYANRGAEEDFK : 175
rat    RUKDSASGLDTAKTYENTVLLSFPSTEQPNSVEVVGPNETVFHSFQPFEKNLTGECAEPNVLQPYAAYAFPGTFKGPLVYYANRGSEDDFK : 180

human  ELCTQGIKLEGTIALTRYGGVGRGAKAVNAAKHGVAGVLVYTDFADINDGLSSPDETFPNSUYLPPSGVERGSYYEYFGDPLTPYLPPAVP : 265
rat    KLEAEGINLKGTIALTRYGSVGRGAKAINAARHGWVGVLVYTDPGDINDCKSLPNETFPNSMGLPPSGVERGSYYEYFGDPLTPYLPPAHP : 270

human  SSFRVDLANVSGFPPIPTQPIGFQDARDLLCNLNGTLAPATUQGALGCHYRLGPGFRPDGDFPADSQVNVSVVNRLELRNSSNVLGIIPG : 355
rat    VSFRLDPENISGFPPIPTQPIGFEDAKNLLCNLNGTSAPDSUQGALGCEYKLGPGFEPNGNFPPAGSEVKVSVVNRLELRNSSNVLGIICG : 360

human  AVEPDRYVLVYGNHRDSUVHGAVDPSSGTAVLLELSRVLGTLLKKGTURPRRSIVFASMGAEEFGLIGSTEFTEEFFNKLQERTVAYINVD : 445
rat    AVEPDRYVIYGNHRDSUVHGAVDPSSGTAVLLEISRVLGTLLKKGTURPRRSIIFASUGAEEFGLIGSTEFTEEFLSKLQERTVTYINVD : 450
```

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FIG. 2. (CONTINUED)

```
human  ISVF AMATLPVQGTPPVVQSVVTSATKEIRSPGPGDLSIYDNWIRYFNRSSPVYGLVPSLGSLGAGSDYAPFVHFLGISSMDIAYTYDRSK : 535
rat    ISVF SMATLRAQGTPPVVQSVIFSATKEISAPGSSGLSIYDNWIRYTMRSSPVYGLVPSNGTLGAGSDYASFIHFLGITSMDLAYTYDRSK : 540

human  TSARIYPTYHTAFDTFDYVDKFLDPGFSSHQAVARTAGSVILRLSDSFLPLKVSDYSETLRSFLQAAQQDLGALLEQHSISLGPLVTAV : 625
rat    TSARIYPTYHTAFDTFDYVEKFLDPGFSSHQAVARTAGSVLLRLSDSFLPLNVSDYSETLQSFLQAAQENLGALLESHNISLGPLVTAV : 630

human  EKFENEAAALGCRISTLQFGSPDDPLQVRIILNDQLMLLEFTFLNPRAFPEERYYSHVLWAPSHGLRSHIPGLSNACSRARDTASGSEAWAE : 715
rat    EKFKLAAAALNCHILTLQKSSPDDPLQVRIIVNDQLMLLEFAFLNPRAFPEERYYSHVLWAPNTASVATFPGLANIYARAQEINSCAEAWAE : 720

human  VQRQLSIVWTALEGAAATLRPVIADLL-- : 740
rat    VERQLSIAWMALEGAAATLCPVTDLL-- : 745
```

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FIG. 3

MQWTKVLGLGLGAAALLGLGIILGHFAIPKKANSLAPQDLDLEILETVMGQLDAHRIRENLRELSREPHLASSPRDEDLVQLLLQRWKDP 90

deletion 1 (bp 497-619) →

ESGLDSAEAXTYEVLLSFPSQEQPNVVDIVGPTGGIIHSCHRTEENVTGEQGGPDVVQPYAAYAPSGTPQ*GLLVYANRGAEEDFKELQTQ* 180

*GIRLEGTIALTRYGGVGRGAKA*VNAAKHGVAGVLVYTDPADINDGLSSPDETFPNSWYLPPSGVERGSYYEYFGDPLTPYLPAVPSSFRV 270

```
gtgagcgtctacaaccgcctggagctgaggaactcttccaagtcctggcatcatccg
tgggctgtggagcctggtgagccctcctcttgctgcctgcacccagccctgctct
gctctgatgccgctgtctcatccctcctcagcctgcctgccaccaccagcccagctccc
cctgcccacctctcctcctccctgttcctcgcccctttcctctgg     ccag
```
insertion at bp 1094

deletion 2 (bp 903-1007) →

DLANVSGFPPIPTQPIGFQDARDLL*CNLNGTLAPATWQGALGCHYRLGPGFRPDGDFPAD*SQVNVSVYNRLELRNSSNVLGIIRGAVEP- 359
                                      G

-------------DRYVLYGNHRDSWVHGAVDPSSGTAVLLELSRVLGTLKK 399

EPSSCCLHPRPLLCSGCRCPHPALPLPPPSPAPPAHLSLSSGSLPLFLWP

GTWRPRRSIVFASWGAEEFGLIGSTEFTEEFFNKLQERTVAYINVDISVFANATLRVQGTPPVQSVVFSATKEIRSPGPGDLSIYDNWIR 489

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FIG. 3 (CONTINUED)

deletion 3 (bp 1525-1615); deletion 4 (bp 1525-1615)

gtgaggaggagagacaaggggcatcctgagacaccaggacaggaggagctgaagactgagccctggccttgtcaccttgccgcag

△ insertion at bp 1697

YFNRSSPVYGLVPSLGSLGAGSDYAPFVHFLGISSMDIAYTYDRSKTSARIYPTYHTAFDTFDYVDKFLDPGFSSHQAVARTAGSVILRL   579
RLQQPSGCGPDSGECDSPAQ*
RARLQPGS PPTTQPLTPLTMWTSFWTRASAAIRLWPGQRGV
EEGDKGHPETRTGEAED*

gtatgcacagccctgaccctgaggtatggggagccctgcaccccccatgactgagccactgcttgttcctcacag

△ insertion at bp 1870

SDSFFLPLKVSDYSETLRSFLQAAQQDLGALLEQHSISLGPLVTAVEKFEAEAAALGQRISTLQKGSPDPLQVRMLNDQLMLLERTFLNP   669
GMHSPDPEVWGALHPHD*

RAFPEERYYSHVLWAPSHGLRSHIPGLSNACSRARDTASGSEAWAEVQRQLSIVVTALEGAAATLRPVADL*   740

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FIG. 4.

```
CTCAAGAAGCCATGGCGGAATCCAGGGGCCGTCTGTACCTTTGGATGTGCTTGGCTGCGCTGGCATCTTTCCTGATGGGATTTATGG
         M  A  E  S  R  G  R  L  Y  L  W  M  C  L  A  A  A  L  A  S  F  L  M  G  F  M  V                90

TGGGCTGGTTTATTAAGCCTCTCAAAGAAACCACTTCTGTGCGCTATCATCAAGTATACGGTGGAAACTGTATCCGAAATGAAAG
G  W  F  I  K  P  L  K  E  T  T  S  V  R  Y  H  Q  S  I  R  W  K  L  V  S  E  M  K  A        180

CTGAAAACATCAATCATTTCTTCGTTCTTTACAAAGCTTCCTCATCTGGCAGGAACAGAACAAAATTCTTTGCTTGCCAAGAAAATCC
E  N  I  K  S  F  L  R  S  F  T  K  L  P  H  L  A  G  T  E  Q  N  F  L  A  K  K  I  Q        270

AAACCCAGTGGAAGAAATTGGACTAGATTCAGCCAAGTTGGTTCATTATGATGTCCTCTATCTTACCCCAATGAGACAAATGCCAACT
T  Q  W  K  K  F  G  L  D  S  A  K  L  V  H  Y  D  V  L  L  S  Y  P  [N] E  T  N  A  N  Y     360

ATATATCGATTGTGGATGAACATGAAACTGAGATTTCAAAAACATCATACCTTGAACCACCAGATGGCTATGAGAATGTTACAAATA
I  S  I  V  D  E  H  E  T  E  I  F  K  T  S  Y  L  E  P  P  P  D  G  Y  E  [N] V  T  N  I      450

TTGTGCCACCATATAATGCTTTCTCAGCCCAAGGCATGCCAGAGGGAGATCTTGTATATGTGAACTATGCCACTGAAGACTTTTCA
V  P  P  Y  N  A  F  S  A  Q  G  M  P  E  G  D  L  V  Y  V  N  Y  A  R  T  E  D  F  F  K     540

AACTAGAAAGAGAGATGGGCATCAACTGTACTGGGAAGAGATTGTTATTGCAAGATATGGAAAAATCTTCAGAGGAAATAAAGTAAAAATG
L  E  R  E  M  G  I  [N] C  T  G  K  I  V  I  A  R  Y  G  K  I  F  R  G  N  K  V  K  N  A     630

CCATGTTAGCAGGAGCCATAGGAATCATCTTGTACTCAGATCCAGCTGACTACTTTGCTCCTGAGGTACAGCCATATCCCAAAGGATGGA
M  L  A  G  A  I  G  I  I  L  Y  S  D  P  A  D  Y  F  A  P  E  V  Q  P  Y  P  K  G  W  N     720

ATCTTCCTGGAACTGCAGCCCAGAGAGGAAATGTGTTAAATTTGAATGGTGCTGGTGACCCACTCACTCCAGGCTATCCAGCAAAAGAAT
L  P  G  T  A  A  Q  R  G  N  V  L  N  L  N  G  A  G  D  P  L  T  P  G  Y  P  A  K  E  Y     810

ACACTTTCAGACTTGATGTTGAAGAAGGAGTTGGAGTCGGAATCCCCGAATACCTGTACATCCCATTGGATATAATGATGCAGAAATATTATTAC
T  F  R  L  D  V  E  E  G  V  G  I  P  R  I  P  V  H  P  I  G  Y  N  D  A  E  I  L  L  R     900

GCTACTTGGGAGGAAATTGCTCCACCAGATAAGAGTTGGAAGGGAGCCCTTAATGTGAGTTATAGTATCGGACCTGGCTTTACAGGGAGTG
Y  L  G  G  I  A  P  P  D  K  S  W  K  G  A  L  [N] V  S  Y  S  I  G  P  G  F  T  G  S  D     990

ATTCTTTCAGGAAGGTTAGAATGCATGTTTATAACATCAATAAAATTACAAGGATTTACAATGTAGTGGAACATCAGAGGATCTGTGG
S  F  R  K  V  R  M  H  V  Y  N  I  N  K  I  T  R  I  Y  N  V  V  G  T  I  R  G  S  V  E     1080

AACCTGACAGGTATGTTATTCTGGGAGGTCACCGGGAGTCGCTCCTGGGTATTTGGAGCTATTGGAGCTGGGTTGCTGTTTGCAAG
P  D  R  Y  V  I  L  G  G  H  R  D  S  W  V  F  G  A  I  D  P  T  S  G  V  A  V  L  Q  E     1170
```

FIG. 4. (CONTINUED 1)

```
AAATTGCCCGGAGTTTTGGAAAAACTGATGAGTAAAGGCTGGAGACCTAGAGAACTATCATTTTGCCAGCTGGGATGCAGAGAGAATTTG   1260
 I  A  R  S  F  G  K  L  M  S  K  G  W  R  P  R  T  I  F  A  S  W  D  A  E  E  F  G

GACTTCTGGGTTCCACAGATGGGCTGAGGAGAATGTCAAAATACTCCAGGAGAGAAGCATTGCTTATATCAACTCGGATTCATCTATAG   1350
 L  L  G  S  T  E  W  A  E  E  N  V  K  I  L  Q  E  R  S  I  A  Y  I  N  S  D  S  S  I  E

AAGGCAATTATACTCTCAGAGTTGACTGTACTCCCCTTCGTTACCAATTAGTGTATAAACTGACAAAAGAGATCCCAGCCCTGATGATG   1440
 G [N] Y  T  L  R  V  D  C  T  P  L  L  Y  Q  L  V  Y  K  L  T  K  E  I  P  S  P  D  D  G

GGTTTGGAGAGTAAATCACTGTATGAAAGCTGGTTGGAAAAAGACCCTTCACCTGAAAATAAAAATTGCCTAGAATCAATAAGCTGGGAT   1530
 F  E  S  K  S  L  Y  E  S  W  L  E  K  D  P  S  P  E  N  K  N  L  P  R  I  N  K  L  G  S

CTGGAAGTGACTTTGAAGCTTATTTTCAGAGACTTGGAATTGCTTCAGGCAGAGCCCGTTACACTAAGAATAAGAAAACAGATAAGTACA   1620
 G  S  D  F  E  A  Y  F  Q  R  L  G  I  A  S  G  R  A  R  Y  T  K  N  K  K  T  D  K  Y  S

GCAGCTACCCAGTGTACCACACAATTTATGAGACATTTGAATTGGTAGAGAAATTTTATGACCCCACATTTAAAAAACAACTTTCTGTGG   1710
 S  Y  P  V  Y  H  T  I  Y  E  T  F  E  L  V  E  K  F  Y  D  P  T  F  K  K  Q  L  S  V  A

CTCAATTACGAGGAGCACTGGTATATGAGCTTGTGTGGATTCTAAAATCATTCCTTTTAATATTCAAGACTATGCAGAAGCTTGAAAAACT   1800
 Q  L  R  G  A  L  V  Y  E  L  V  D  S  K  I  I  P  F  N  I  Q  D  Y  A  E  A  L  K  N  Y

ATGCAGCAAGTAGTCTATAATCTATCTAAGAAGAACATGATCAACAATTAACAGACCATGAGTATCATTTGACTCCTTATTTCTGCTGTGA   1890
 A  A  S  I  Y [N] L  S  K  K  H  D  Q  Q  L  T  D  H  G  V  S  F  D  S  L  F  S  A  V  K

AAAACTTCTCAGAGGCTGCTTCAGATTTTCATAAACGACTTATACAAGTTGATCTTAACAATCCATTGCAGTGAGAATGATGAATGACC   1980
[N] F  S  E  A  A  S  D  F  H  K  R  L  I  Q  V  D  L  N  N  P  I  A  V  R  M  M  N  D  Q

AACTGATGCTCCTGAAAGAGCATTCATCGATCCTCTCTGGTTTACCAGGAAAGCTGTTCTATAGGCACACATCATATTGCTCCAAGTAGCC   2070
 L  M  L  E  R  A  F  I  D  P  L  G  L  P  G  K  L  F  Y  R  H  I  I  F  A  P  S  S  H

ACAACAAATATGCTGGAGAATCATTCCCTGGAATCTATGATGCTATCTTTGATATTGAAAATAAGGCCAACTCTCGTTGGCTGGAAAG   2160
 N  K  Y  A  G  E  S  F  P  G  I  Y  D  A  I  F  D  I  E  N  K  A  N  S  R  L  A  W  K  E

AAGTAAAGAAACATATTTCTATTGCAGCTTTTACAATTCAAGCAGCAGGAACTCTGAAAGAAGTATTATAGAAGGTCTCAAGTGGCT   2250
 V  K  K  H  I  S  I  A  A  F  T  I  Q  A  A  A  G  T  L  K  E  V  L  .
```

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FIG. 4. (CONTINUED 2)

```
AGCCATTAAAGGTGTTGCTAAAAGTCTGAGGATAAAATTCACCTTTCTGATAACTTATGAAGCCAGGGTGTTCTAAACTCTTTTCATGTC    2340
ATGTTTTGATTATAGGCTTTGGTCTTTTCATCTGCAAAGCCTTTTTTTTTTTTGCTCTTTAAAAGTTAATAATTATATTAGCAAAGTGTT    2430
AATCTAATGAAGTAAAAAACTCCGTGTGGCAGAAGAGTAAAAGAAAATTCCCTAAATTATAGCAAGGAACATGAATTCTCAGACACATTGTG    2520
AGTGTGGGAATGTAAAATCACTTTTGAAAACAGTTTGAAAAACAGTTTCCTATAAAGTAAACATACACTTTTACTTTAGGACTCC    2610
AGAATTCCACTTCTAGTTATTTATTCAAGAGAAGGAAAAACAATGATCACAGCAATACTTGTATGCATGTTCATTGCAACTTAAAAAGCGT    2700
AAAAACCCCAAATGTCCATCCACAGACGAATGTATAAACTGTGGTATCCATTACACAATAGACTACTTACTACTCAGCAATAAAAATGAA    2790
GTAACTTTCAATAAATGCAATATTATTGGCAGACATTGTTGAAGGAAAAAAGCCAGACAAACAACTACATAAAATATGTTTCTATTTAGA    2880
TGAAGTGGCAAACTAATCTGTAGTGTTAAAAATTAGTGATGATTGCCTGGGCCAAGTGGCAGGTTGGGGAGGATGGCTGCAAAGAAGT    2970
ATGAGGAAACTTTCTCCAATAGATGAGAATTTTCCGTATCTTGATCTGAGTGGCAAATTGTAAACTTAAAATATATATAAAAATTTATTGA    3060
AAGAAAATTAAGCCTCAATAAACGTGATTATAAAAAAAAAAAAAAAAAAGG    3110
```

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FIG. 5.

```
CGGCGCGGAGGGCCCCAGCCAGTCAGGGGTGTGGCCGCGCCGCCACCGTAAGGCTAGGCCGCTTAGTCCTGGGAGCCGCCTCCGTCG        90

CCGCCGTCAGAGCCGCCCTATCAGATTATCTTAACAGAAACCAACTGAAAAAAATGAAATTCCTTATCTTTCGCATTTTTCGGTGG         180
                                                      M  K  F  L  I  F  A  F  F  G  G

TGTTCACCTTTTATCCCTGTCTCTGGAAAGCTATATGCAAGAATGCATTCTTAAGAGGACTTTTGAAGAAATAAAGAGAAATAGC         270
 V  H  L  S  L  C  S  G  K  A  I  C  K  N  G  I  S  K  R  T  F  E  E  I  K  E  E  I  A

CAGCTGTGGAGATGTTGCTAAAGCAATCATCAACCTAGCTGTTTATGGTAAAGCCCAGAACACAGATCCTATGAGCGATTGGCACTTCTGGT   360
 S  C  G  D  V  A  K  A  I  I  N  L  A  V  V  G  K  A  Q [R] S  Y  E  R  L  A  L  L  V

TGATACTGTTGGACCCAGACTGAGTGGCTCCAAGAACCTAGAAAAAGCCATCCAAATTATGTACCAAAACCTGCAGCAAGATGGCTGA        450
 D  T  V  G  P  R  L  S  G  S  K  N  L  E  K  A  I  Q  I  M  Y  Q  N  L  Q  Q  D  G  L  E

GAAAGTTCACCTGGAGCCAGTGAGAATACCCCACTGGGAGAGGGGAGAATCAGCTGTGATGCTGGAGCCAAGAATTCATAAGATAGC        540
 K  V  H  L  E  P  V  R  I  P  H  W  E  R  G  E  E  S  A  V  M  L  E  P  R  I  H  K  I  A

CATCCTGGGTCTTGGCAGCAGCATTGGGACTCCTCCAGAAGGCATTACAGCAGAAGTTCTGGTGGTGACCTCTTTCGATGAACTGCAGAG     630
 I  L  G  L  G  S  S  I  G  T  P  P  E  G  I  T  A  E  V  L  V  V  T  S  F  D  E  L  Q  R

AAGGGCCTCAGAAGCAAGAGGGAAGATTGTTGTTTATAACCAACCTTACATCATCAAGACGGTGCAATACCGAACGCAGGGGGC        720
 R  A  S  E  A  R  G  K  I  V  V  Y  N  Q  P  Y  I [N] Y  S  R  T  V  Q  Y  R  T  Q  G  A

GGTGGAAGCTGCCAAGGTTGGGGCTTTGGCATCTCCATTCGATCCGTGGCCTCCTTCTCCATCTACAGTCCTCACACAGTATTCAGA        810
 V  E  A  A  K  V  G  A  L  A  S  L  I  R  S  V  A  S  F  S  I  Y  S  P  H  T  G  I  Q  E

ATACCAGGATGGCGTGCCCAAGATTCCAACAGCCTGTATTACGGTGGAAGATGCAGAAATGATGTCAAGAATGGCTTCATGGGATCAA       900
 Y  Q  D  G  V  P  K  I  P  T  A  C  I  T  V  E  D  A  E  M  M  S  R  M  A  S  H  G  I  K

AATTGTCATTCAGCTAAAGATGGGGGCAAAGACCTACCCAGATACTGATTCCTTCAACACTGTAGCAGAGATCACTGGGAGCAAATATCC      990
 I  V  I  Q  L  K  M  G  A  K  T  Y  P  D  T  D  S  F  N  T  V  A  E  I  T  G  S  K  Y  P

AGAACAGGTTGTACTGGTCAGTGGACATCTGGACAGCTGGGATGTTGGGCAGGGTGCCATGGATGATGGCGGTGGAGCCTTTATATCATG     1080
 E  Q  V  V  L  V  S  G  H  L  D  S  W  D  V  G  Q  G  A  M  D  D  G  G  G  A  F  I  S  W

GGAAGCACTCTCACTTATTAAAGATCTTGGGCGTCTCAAAGAGGACTCTGCGGCGTCGACTGCAGAGAACAAGGTGGAGT        1170
 E  A  L  S  L  I  K  D  L  G  L  R  P  K  R  T  L  R  L  V  W  T  A  E  E  Q  G  G  V
```

FIG. 5. (CONTINUED)

```
TGGTGCCTTCCAGTATTATCAGTTACACAAGGTAAATATTTCCAACTACAGTCTGGTGATGGAGTCTGACGCAGGAACCTTCTTACCCAC    1260
  G  A  F  Q  Y  Y  Q  L  H  K  V  N  I  S  N  Y  S  L  V  M  E  S  D  A  G  T  F  L  P  T

TGGGCTGCAATTCACTGGCAGTGAAAAGGCCAGGCGCCATCATGGAGGAGGTTATGAGCCTGCTGCAATATCACTCAGTCCT          1350
  G  L  Q  F  T  G  S  E  K  A  R  A  I  M  E  E  V  M  S  L  L  Q  P  L  N  I  T  Q  V  L

GAGCCATGGAGAGGGACAGACATCAACTTTTGGATCAAGCTGGAGTGCCTGGAGTCCAGTCTACTTGATGACTTATACAAGTATTTCTT    1440
  S  H  G  E  G  T  D  I  N  F  W  I  Q  A  G  V  P  G  A  S  L  L  D  D  L  Y  K  Y  F  F

CTTCCATCACTCCACGGAGACACCATGACTGTCATGGATCCAAAGCAGCAGATGAATGTTGCTGCGTGTTGGGCTGTGTTGTTTCTTATGT  1530
  F  H  H  S  H  G  D  T  M  T  V  M  D  P  K  Q  M  N  V  A  A  A  V  W  A  V  V  S  Y  V

TGTTGCAGACATGGAAGAAATGCTGCCTAGGTCCTAGAAACAGTAAGAAAGAAAACGTTTCATGCTTCTGGCCAGGAATCCGGGTCTGC    1620
  V  A  D  M  E  E  M  L  P  R  S  *

AACTTTGGAAAACTCCTCTTCACATAACAATTTCATCCAATTCATCTTCAAAGCACAACTCTATTTCATGCTTTCTGTTATTATCTTTCT    1710

TGATACTTTCCAAATTCTCTGATTCTAGAAAAAGGAATCATTCTCCCCTCCCACCACATAGAATCAACATATGGTAGGGATTACAG      1800

TGGGGGGCATTTCTTTATATCACCTCTTAAAAAACATTGTTTCCACTTTAAAAGTAAACACTTAATAAATTTTGGAAGATCTCTG        1884
```

FIG. 6.

```
NAALAD I    MWNILHETDSAVATARRPRWLCAGAIVLA-GGFFLGFLFGWPIKSSNEATNLTPKHN-K-AFTDSTKLENINKFLYNFTQIPHLAGTEQ    88
NAALAD L    --------MGWTKVLGLGLGAAALGLGILGILGHPAIPKKANSLAP----QDLDIELETVLGLDAHRIPENLRELGREHLASPR         75
NAALAD II   --------MAESLRLYIWMCLAAFLASFLWGFMVGWFIKPLKET-SLRYHQSLRWKLENLNSFLRSPTKLPHLAGIEQ              78
NAALAD IV   -------MKFLIPAFFGEVHLLSLC3GKAICKNG-SKRTPEEIKEEIASCGDLAKAIINLAVYGKAQNRSYERLALLVDTLVGERLSSKN  83
```

```
NAALAD I    NPQJAKCIQSQMT--IEFELDLSYENKTHPLYISINEDGNEIFNTLFPLEPEYLNVSQLTVPFSASSPCLMPBGDEVYL               176
NAALAD L    DEDIVQLLQRMPDPLSSLDLAEAXTLENILSFPSLEQPLVVDIVGPTGGIIHSCHRTLENVTESGGPDVVQFYAAYAPSSTPRSELGVI     165
NAALAD II   MFLIAKKIQTQAN--KFSLISAKIVHLDYLLSYENETNANLYISISDEHETEIFKTSYLPEDLYENVTLIYPRNMFSACELPEGDLVYI     166
NAALAD IV   LEKAIQIHYQNLQ--IDEIEKVHLEPVRLPHWERGLEPRIHKIAILGLGLSIGTPEE                                     145
```

```
NAALAD I    VNYARTEDFFRLERDLHKINCSGKIVLAPSLEKYFRGNELVRNTAQLAGAKEVILNSDPADYLEAPGLKS---MPDEWNLEGGGVPRENLNLNG  263
NAALAD L    AFLRG--ALEDPRELQTQGIKLESTIALTPLEGLRGLRGAHAVMILAKHLSVAEVILVVTDPEALINDGLS3PDETMPNSLYLPSGVERESYYEY--  252
NAALAD II   VNYARTEDFFRRLEREYGINCLGKIVLAPSLEKYFRGNMLVRIGMLAEAILHYSMDPALIYSAPEVQP---NLKCLNLLGTAAGKRSMNLNLNG  253
NAALAD IV   ----STAELLVTSPDELQRPASE-ARGK---LVVINQEYINJSRTLVQY---RTCGAVEAAKVGALASILRSVA                        208
```

```
NAALAD I    AGDPLTEGYPANEALAFRGLABAVFLSIEVHFPIGLYDASKLIEKYGLSAPEDSGHRESIKVPINVGFSFTGNF---STQKLKLRHHSTN  350
NAALAD L    FGDPITPYLRAVPSSLRVDIANVSFFPIFTQPIFFQDARDLMCNMLTLAE-AUEQEALGCHLRLGPSFERPDGDFPADSQVNSLYNRL     341
NAALAD II   AEDPLTPGYENKEVTFRLDLEEGVFPRLHEIGYNDAPILLRYLGSIAPEDKNMAAJNVSLSIGLEGETG3D---SFRKLVRLHLYNIN     340
NAALAD IV   SFSIYSLHTGIQLQD----SLEKLETACLTVEDASMLSRMASHGIKIVIQLRMGAKTYPDTD9                               268
```

similar to bacterial Zn^{2+} dependent peptidase

```
NAALAD I    EVTRILWLJISTLRGAUEPDRYVILGLSHRDSM--SGLDEQLRAUWYHSEHVLSFFLEKKEF-IRFRKTLLFASMDLSEEFLEJLIGSTEWLAEE  437
NAALAD L    ELRNSSRLLEIIRLAUEPDRLVIYSNHRDSM--VH--SAVEPSLETLVILELSRLVLSTLLKKLT-IRPRRSIVPASMGLAEEFLELIGSTEFTEE     429
NAALAD II   KLTRILVLVETIRSSVEPDRNVILSLHPDSM--VF--SAIDETLSLVLVIQELARLSPLKLMSKE-JRFRRTIIPASMDLAEEFLELIGSTEWLAEE    427
NAALAD IV   SMTLAEITLSKYLEQVLVSEHLIDSMLVGQSAMIDGGLA---PISWEALSLRLKDLF-LRPKRTIRLVLTLABECGVGAFNLY-              348
```

FIG. 6. (CONTINUED)

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FIG. 7

Growtree Phylogram of: naaladase_short.distances, Tree Tree_1
June 17, 1998 17:46

NAALADase_I_human

NAALADase_I_rat

NAALADase_II_human

NAALADase_L_human

NAALADase_L_rat

NAALADase_IV_human

FIG. 8

```
NAALAD I    DAQKLIEKMGGSAPPD-SSURGSLKVPINVGPFTGNF---STQKVKCHIHSTNEVTRIYNWIGTLREAVEPDRYVILGG    375
NAALADL     DAEILLRYLGGIAPPD-KSUKGALNVSSIGPGFTGSD---SFRKVRCHVYNINKITRIYNWVGTIRGSVEPDRYVILGG    366
NAALAD II   --RDLCNLNGTLAP--ATWQGALGCHLRLGPGFRPDGDFPADSQVNUSVYNRLELRNSSWLGIIRGAVEPDRYVLYGN    367
NAALAD IV   SPHTGIQEYQDGVPKIPTACITVEDAEHHSRMASHGIK---IVIQLKCGAKTYPDTDS-FNDVAELIESKYPEQVLVSG    289
APE 3 yeast ----------TKHTVATVGVPYKVGKKLIANIALNIDYSLYFAMDSYVEFIKTQVIIADTKHG-DPLNIVALGA      313
P96152      QITNTIRALSSFNNRFYTTASGAQASDMLANEURSLIS--SLPGSRIEQIKHSGYNQ-KSVVLTICQSEKPDEVIVGG     199
AMPX vibpr  QITGTISSLESFTNRFYTTTSGAQASDWIASEUQALSA---SLPNASVKQVSHSGYNQ-KSVWMTITGSEAFDEWVISG     202
APX Strgr   -----------NNGGNR--AHGRPGYKASVDYVKAKLDAA----GYTTTLQQFTSGGATG-YNLIANUPEG-DFNKVLIAAA      84
```

← ★

```
NAALAD I    HRDSW-WF------C--EI-DPQSG-BAV-VHEIVRSFGTL-KKEG--URPRRTILFASWDAEEFGLLGSTEWA-EE-NS      439
NAALADL     HRDSW-WF------G--AI-DPTSG-VAV-LQEIAMSFGKL-MSKG--URPRRTIFASWDAEEFGLLGSTEWA-EE-NV      429
NAALAD II   HRDSW-WH------SAV--DPSSGTUVL-L-ELSWVGTLLK-KGTUFPRRSIVFASWGAREEFGLIGSTEFT-EEFFN      432
NAALAD IV   HLDSUDV------SQGAMDDGGE-QFISW-EALSLI---KDLG-LRPHRTLRLVLUTHEEQGGWGAFQWY-QLHKV      352
APE 3 yeast HSDS---VEE------SPGINDDGECTISL-L-NUARQLTH-----FKINNKVRFAWMAEEEGLLGSNFWAYNLTKE      375
P96152      HLDST-LGSHTNEQSIAPEADDDASGIWSL-S-EIIRVL-----RDNN--FRPKRSAALMAVAREEVGLRGSQDPA-NQYKA      270
AMPX vibpr  HLDST-IGSHTNEQSVAPEADDDASGIRAV-T-EVIFVL----SENN--FQPKRSIAYMAVAREEVGLRGSQDLA-NQYKS      273
APX Strgr   HLDS---USS------SAGINDNGSCSDAU-L-ETALAU-----SRAG--VQPDRHLRSAUWGAREELGLIGSKFWV-NNLPS      147
```

★ ★

```
NAALAD I    RLLQERGVAYINADSSI-EGNYTLRUDCUPLMYSLVHNLIKELKSPDEGFEGKSLYESUTKKS--PSPEFSGMPRISKLS      516
NAALADL     KILQERSIAYINSDSSI-EGNYTLRUDCUPLLYQLVYKLIKEIPSPDDGFESKSLYESULEKD--PSPENKNLPRINKLS      506
NAALAD II   KL-QERTVAYINVDISV-FANATLRUQGUPPVQSVVFSAUKEIRSPGPGD--LSIYDNUIRYFNRSSPVYGLVPSLGSLS      508
NAALAD IV   NIS--NYSLVMESCAGT-FLPTGLQFTGSEKARA----IHEEVM-------SLLQPLNITQ------VLSHG      404
APE 3 yeast ENSKIR--VFUDYDMMA-SPNYEYEUYDANNKENP--KGSEELK-------NLYVDUYKAH------HLNYTLVPFDG      435
P96152      QGK--KVVSVULQLDMTNYRGSAEDIUFIUDYTDS---NLUQFLT-------TLIDEULPEL----YDRCE      327
AMPX vibpr  EGK--NVVSAUQLDMTNYKGSAQDVVFIUDYTDS---NFUQYLT-------QLMDEULPSL----YDG------FDTCE      330
APX Strgr   AD-RSILAGYLNFDM-IGSPNPGYFUYDDDPVIEK--TFKNYFAG-----LNVPTEIETE----GDGRSDHAPFKN      210
```
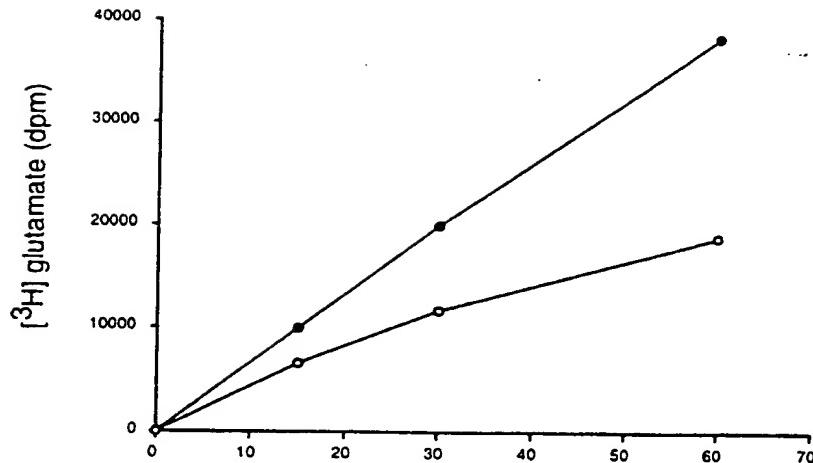
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FIG. 8. (CONTINUED)

```
                                                                                        *
NAALAD I    SGNDFEVFQRLEIASGRARYTNUETNKFSGYPLYVVEYYELVEK-----FYDPMKYH-LTVQVRGG------    582
NAALADL     SGSDFEAYQRLGIASGRARYTNKKKTDKYSSYPVYIYEFELVEK-----FYDPTKKQ-LSVQLRGA------    572
NAALAD II   AGSDYAPFVHFLEISSMDIAYTYDRSKTSARIYPTYHAFDTFDYVDK----FLDPGHSSH-QAVERTAGS------  574
NAALAD IV   EGTDIN-FUIQAEVPGASLLDDLYKYFF-----FHHSHGDVMTVHDPKQMNVAAAVLAVVSYVVEDMEEMLPRS----  472
APE 3 yeast RSDYVGFINNGIPAGGIATGAERNNVNNGKVLDRCYHQLCDDVSNLSUDAFITNTKLIAHSVATYLDSFEGFPKRETQKH 515
P96152      YACSDHASHHKAEFSAAMPFESHFKDYN-----PKIHUSQULANSDPT--GNHAVTTKLGLAYVIEMAN------      391
AMPX vibpr  YACSDHASHHNAEYPAAMPFESKFNDYN-----PRIHUTQDLANSDPT--GSHAKKUTQLGLAYLIENGS------     394
APX strgr   VGUPVGGLHTGAEYTKSAAQAQRUGGTAGQAFDRCYHESCDELSNHNDTALDRNSDAAAHAIUTLSSGTGEPPT------ 294
```
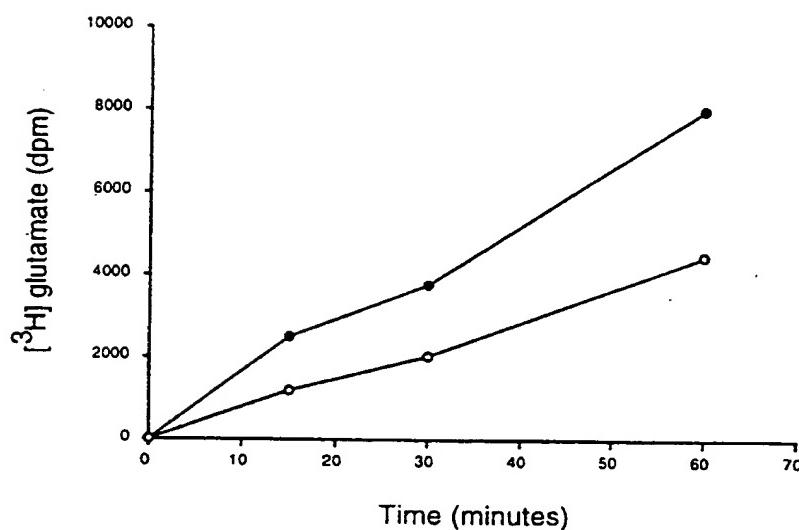
A

FIG. 9.

B

Time (minutes)

C

Quisqualate concentration (log M)

SUBSTITUTE SHEET (RULE 26)

FIG.10.

A

B

FIG. 11.

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FIG.12

A

B

FIG. 13.

A

B

C

D

E

SUBSTITUTE SHEET (RULE 26)

FIG. 14.

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FIG. 15.